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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/664,697	09/16/2003	Cheng Li		5503
7590	12/23/2008		EXAMINER	
CHENG LI INCUBE 1390 WILLOW ROAD MENLO PARK, CA 94025			GUPTA, ANISH	
		ART UNIT	PAPER NUMBER	1654
		MAIL DATE	DELIVERY MODE	12/23/2008 PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/664,697	LI ET AL.	
	Examiner	Art Unit	
	ANISH GUPTA	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 14 July 2007.

2a) This action is **FINAL**. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 5,6,10-13,18-22,25 and 27-33 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 5,6,10-13,18-22,25 and 27-33 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some * c) None of:

- Certified copies of the priority documents have been received.
- Certified copies of the priority documents have been received in Application No. _____.
- Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____.

4) Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.

5) Notice of Informal Patent Application

6) Other: _____.

DETAILED ACTION

1. The amendment filed, Oct. 19, 2007 is acknowledged. Claims 5-6, 18, 19, 25, 28, and 29 were amended, claims 3-4, 9, 23-24 and 26 were canceled and 30-33 were added. Claims 5-6, 10-13, 18-22, 25, 27-33 are pending in this application.

Election/Restrictions

2. Applicants have stated that Applicants previously elected the species (NH2-GLY-THR-PRO-GLY-PRO-GLN-GLY-ILE-ALA-GLY-GLN-ARG-GLY-VAL-VAL)4-(Lys)2-Lys- β -Ala-COOH and not NH2-GLY-THR-PRO-GLN-ILE-ALA-GLY-ARG-GLY-VAL-VAL)4-(Lys)2-Lys- β -Ala-COOH.. Applicants are correct and the citation in the previous office action was a typographical error. This is evidenced by the fact that the GTPGPQGIAGQRGVV was the peptide used to reject the claims.

Maintained Rejections

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was

commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 5-6, 10-13, 18-22, 25, 27-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dang et al. (US2003/0113478) in view of Tam (Peptides: synthesis, structures, applications).

The claims are drawn to a peptide comprising a MAP structure conjugated to a substrate.

The reference of Dang et al. teach stents and grafts and means of coating them with a peptide. The reference specifically disclose coating a substrate with the sequence GTPGPQGIAGQRGVV (called P-15) have the ability to provide enhanced endothelial cell growth in vitro. The example characterized the P-15 surface treatment on ePTFE graft material, and measured its biological activity on the adhesion, migration and proliferation of endothelial cells in vitro. Also shown is the level of P-15 treatment degradation after simulated aging. The results show that this treatment method, characterized by the covalent attachment of a cell-adhesion peptide, was shown to be clean and stable. The surface treatment one PTFE grafts promoted the migration and proliferation of healthy endothelial cells. (see paragraph [0093]). The reference also states that the nature of the substrate to be coated may vary widely. At least a portion of at least one surface of the substrate 10 is coated with the functional group 16 or surface-modifying group 18 of the present invention. Preferably, the entire surface is coated with the functional group 16 or surface-modifying group 18. Suitable substrate materials include all non-porous or porous polymeric substrates, such as polyurethanes, polyamides, polyesters and polyethers, polyether-blockamides, polystyrene, polyvinyl chloride, polycarbonates, polyorganosiloxanes, polyolefins, polysulfones, polyisoprene,

polychloroprene, polytetrafluoroethylene (PTFE), polysiloxanes, fluorinated ethylene propylene, hexafluoropropylene, polyethylene, polypropylene, nylon, polyethyleneterephthalate, polyurethane, silicone rubber, polysulfone, polyhydroxyacids, polyimide, polyamide, polyamino acids, regenerated cellulose, corresponding copolymers and blends, and also natural and synthetic rubbers. A substrate of particular interest to the present invention is expanded PTFE (ePTFE) (see paragraph [0057]).

Note that these meet the limitation of claim 4. The difference between the prior art and the instant application is that the reference does not disclose the MAP structure.

However, Tam teaches the synthesis and Application of branched peptides. The reference disclose the MAP structure where the Z variables are Lysine residues the dimeric (MAP2), tetrameric (MAP4), or octameric (MAP8) lysines are conjugated to a beta alanine residue (see page 458). The reference discloses that numerous peptides have been incorporated into MAP structures, differing in length and size (See table II). The reference disclose that MAP structure can be applied in immunoassays, seradioagnosis, epitope mapping, inhibitors, artificial proteins, and various biochemical studies and purification methods (see page 474). The reference states, as inhibitors, branched peptides with clustered positive charges can lead to stronger binding than their monomers by allowing multiple points of contact (see page 476). Clustering could be achieved by adsorptoin on a surface or by coupling to a carrier or sepharose bead (see page 476). Observations of increased binding of branched peptides to cell surfaces, relative to the monomer, have been observed (see page 476).

It would have been obvious to one of ordinary skill in the art to incorporate the peptide GTPGPQGIAGPRGVV into a multimeric peptide structure (MAP) because branched peptides with clustered positive charges can lead to stronger binding than their monomers by allowing multiple points of contact and MAPs have increased binding of to cell surfaces, relative to the

monomer. Note that the primary reference disclose that the peptide promoted the migration and proliferation of healthy endothelial cells. There would have been a reasonable expectation of success because MAP branched peptides have been shown to have increased binding of to cell surfaces. Tam teaches that the Clustering, which allows for stronger binding than their monomers by allowing multiple points of contact could be achieved by adsorption on a surface or by coupling to a carrier or sepharose bead. Finally, Tam teaches numerous MAP structure and the means of making such structures.

4. Claims 3, 5, 10-13, 18-22, 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bhatnagar (WO9102537) in view of Tam (Peptides: synethesis, structures, applications).

The claims are drawn to a peptide comprising a MAP structure conjugated to a substrate.

The reference of Bhatnagar et al. teach the peptide GTPGPQGIAGQRGVV (called P-15) (see abstract). The reference discloses that the peptide is useful in promoting vertebrate cell adhesion to a substrate when the substrate is coated with the peptide (see page 4 of the reference). The reference also states that the peptide can be used to raise monoclonal antibodies against the epitopic region defined by P-15 (see page 10). Regarding the use for promoting vertebrate cell adhesion, the peptides are attached to a substrate such as glass, plastic, ceramics, organic polymers, gels, silica (see page 11). The reference discloses the means of covalently lining the peptide to the substrate (see page 11). The difference between the prior art and the instant application is that the reference does not disclose the MAP structure.

However, Tam teaches the synthesis and Application of branched peptides. The reference disclose the MAP structure where the Z variables are Lysine residues the dimeric (MAP2), tetrameric (MAP4), or octameric (MAP8) lysines are conjugated to a beta alanine residue (see page 458). The

reference discloses that numerous peptides have been incorporated into MAP structures, differing in length and size (See table II). The reference disclose that MAP structure can be applied in immunoassays, seradioagnosis, epitope mapping, inhibitors, artificial proteins, and various biochemical studies and purification methods (see page 474). The reference states, as inhibitors, branched peptides with clustered positive charges can lead to stronger binding than their monomers by allowing multiple points of contact (see page 476). Clustering could be achieved by adsorption on a surface or by coupling to a carrier or sepharose bead (see page 476). Observations of increased binding of branched peptides to cell surfaces, relative to the monomer, have been observed (see page 476).

It would have been obvious to one of ordinary skill in the art to incorporate the peptide GTPGPQGIAGPRGVV into a multimeric peptide structure (MAP) because branched peptides with clustered positive charges can lead to stronger binding than their monomers by allowing multiple points of contact and MAPs have increased binding of to cell surfaces, relative to the monomer. Note that the primary reference disclose that the peptide is useful in promoting vertebrate cell adhesion to a substrate when the substrate is coated with the peptide. There would have been a reasonable expectation of success because MAP branched peptides have been shown to have increased binding of to cell surfaces. Tam teaches that the Clustering, which allows for stronger binding than their monomers by allowing multiple points of contact could be achieved by adsorptoin on a surface or by coupling to a carrier or sepharose bead. Finally, Tam teaches numerous MAP structure and the means of making such structures.

Response to Arguments

For both rejections, Applicants argue similar points and have been addressed below.

Tam teaches away from the invention because Tam teaches "MAP structure produces an inhibitor due to branched peptides with clustered positive charges. Thus, from the teaching of Tam, one would expect that including GTPGPQGIAGQRGVV in a MAP structure would produce an inhibitor rather than the agonist recited by the present claims."

Applicants arguments have been fully considered but have not been found persuasive.

Applicants reading of Tam seems to be confined to a single page within the reference. However, the teaching of Tam is applicable to not only inhibitors but also other biological peptides. While the reference states that there is increased binding of branched peptides to proteins or cell surfaces compared that of native protein has been exploited for applications as inhibitors. However, this would not lead one to conclude that MAP peptides can only be utilized in inhibitors. Rather, reading the reference, one would be lead to believe that increased binding of branched peptides to proteins or cell surfaces compared that of native protein would be observed in all peptides not only inhibitors. The reference states MAP structure can be applied in immunoassays, seradioagnosis, epitope mapping, inhibitors, artificial proteins, and various biochemical studies and purification methods (see page 474). Thus, MAP structures can be used for any peptide including the one taught by Dang and Bhatnagar.

Rejections are maintained.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the

THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anish Gupta whose telephone number is (571)272-0965. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can normally be reached on (571) 272-0562. The fax phone number of this group is (571)-273-8300.

/Anish Gupta/
Primary Examiner, Art Unit 1654